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## Formulating Microemulsions that Decontaminate a Toxic Substance \*

F.M. Menger  
A.R. Elrington

I have before me a pencil. It may be regarded as a "system" in that several components work in concert to produce a useful object. There is a wood shaft with a graphite core ; a metal band attached to a rubber eraser ; and yellow paint covers the wood. Some components are more useful than others. For example, the graphite is necessary for the pencil to function, but the paint is of secondary importance. The point is that multiple components operate cooperatively to produce something better than available from a single component alone. And so it is with systems on a molecular scale. Chemists have discovered that groups of molecules can perform useful tasks that are unachievable from "single molecule" chemistry (Nature, with its incredibly complex system, the cell, has of course discovered this long ago).

It is my purpose to describe here a multi-component system that is remarkable in its ability to destroy mustard, a highly dangerous compound being produced worldwide. Operation of the system depends on water, hydrocarbon, surfactant, cosurfactant, oxidant, and mustard working in concert within an array of self-organizing molecules [1]. Destruction of mustard is rapid, cheap, selective, and mild.

Our research group has over the years examined a variety of organic systems including micelles, films, water pools, vesicles, laminates, polyaphrons, polymeric systems, and microemulsions. This work is reviewed in a recent *Angewandte Chemie* [2]. In the present article, I will focus on only one type of system, the microemulsion. Since there may be many readers who are unfa-

miliar with microemulsions, I will begin by briefly describing what they are and why they attracted our attention.

A microemulsion is an isotropic and optically clear dispersion of oil-in-water (O/W) or water-in-oil (W/O) where "oil" is a hydrocarbon [3, 4]. The name "microemulsion" derives from the fact that oil droplets in O/W systems, and water droplets in W/O systems, are small (50-500 Å). Microemulsions are thermodynamically stable, and they remain clear indefinitely. They form spontaneously when the following four components are mixed in specific proportions : water, oil, surfactant, and cosurfactant (generally a low molecular weight alcohol). *Figure 1* shows the structure of an O/W microemulsion. The presence of cosurfactant is critical to reducing the interfacial tension between droplets and continuous phase to near zero. In the absence of cosurfactant at the droplet interface, the emulsions become unstable and milky owing to the creation of much larger droplets.

How does one know what proportion of the four components to use ? It is possible, of course, to take microemulsion recipes from the abundant literature on the subject. We found it just as simple to develop our own by "titration". Thus, microemulsions were prepared on a 100 gram scale by weighing a mixture of alcohol, surfactant, and hydrocarbon into a 250 mL Erlenmeyer flask. This white slurry was swirled into a smooth paste. Water was then added with mild agitation to achieve clarity. A few minutes sonication was used occasionally to hasten the process. *Table 1* gives the percentage composition by weight of nine

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Department of Chemistry, Emory University, Atlanta, Ga. 30322, USA.

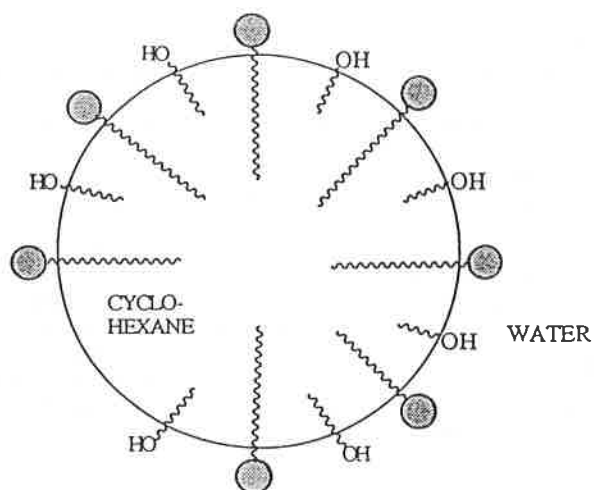


FIGURE 1. - Schematic of an oil-in-water microemulsion where the surfactant head-groups (shaded circles) and the hydroxyls of the cosurfactants lie at the oil/water interface.

microemulsions examined in our work.

Let us examine the features of Table I. ME-1, containing 3 % n-hexane and 82 % water, can be reasonably regarded as an O/W microemulsion in which hexane droplets are dispersed in water. An anionic surfactant (sodium dodecyl sulfate) and an alcoholic cosurfactant (1-butanol) serve as the dispersant. ME-9 is, no doubt, a W/O microemulsion. When the amount of water and oil are similar, there can be uncertainty as to the O/W or W/O identity of the microemulsion. Note that three types of surfactants (anionic, cationic, and neutral) were used to make the microemulsions as exemplified by SDS, CTAB, and Brij-96, respectively (see table legend for definitions of acronyms). Cosurfactants consisted of propanol, butanol, pentanol, or hexanol. In one case, Me-7, the microemulsion is exceptional in that it contains no cosurfactant at all. More will be said later of this microemulsion because it was important in mechanistic considerations.

TABLE I. - Percentage composition by weight of nine microemulsions<sup>a</sup>.

ME	Water	Hydrocarbon <sup>b</sup>	Surfactant <sup>c</sup>	Cosurfactant <sup>d</sup>
1	82.1	3.2 C <sub>6</sub>	4.9 SDS	9.8 B
2	68.9	10.9 C <sub>12</sub>	10.9 SDS	9.3 P
3	60.0	4.0 C <sub>16</sub>	18.0 CTAB	18.0 B
4	60.0	4.0 C <sub>16</sub>	23.6 Brij-96	12.4 B
5	29.6	11.9 nC <sub>6</sub>	0	58.5 iPr
6	28.0	5.0 nC <sub>6</sub>	37.0 CTAB	30.0 B
7	15.1	67.8 C <sub>7</sub>	17.1 AOT	0
8	10.0	41.3 nC <sub>6</sub>	0	48.7 iPr
9	5.3	79.9 C <sub>6</sub>	4.9 SDS	9.8 B

<sup>a</sup> For data on 18 other microemulsions, see A.R. Elrington, "Rapid Deactivation of Mustard in Microemulsion Technology", Ph. D. Thesis, Emory University, 1990.

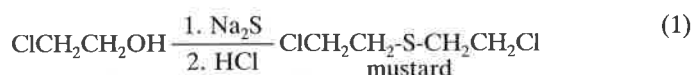
<sup>b</sup> C<sub>6</sub> = cyclohexane; nC<sub>6</sub> = n-hexane; C<sub>7</sub> = n-heptane; C<sub>12</sub> = n-dodecane; C<sub>16</sub> = n-hexadecane.

<sup>c</sup> SDS = sodium dodecyl sulfate; CTAB = cetyltrimethylammonium bromide; Brij-96 = CH<sub>3</sub>(CH<sub>2</sub>)<sub>7</sub>CH = CH(CH<sub>2</sub>)<sub>8</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>10</sub>OH; AOT = 1,4-bis(2-ethylhexyl) sodium sulfosuccinate.

<sup>d</sup> B = 1-butanol; P = 1-pentanol; iPr = 2-propanol.

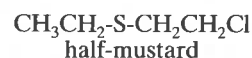
The only compound of the 4-component microemulsion that cannot be structurally altered is water. Since a wide selection of oils, surfactants, and cosurfactants are available, and since their relative concentrations can be varied almost continuously, an inexhaustible assortment of microemulsions are possible. The microemulsions in Table I were formulated rather arbitrarily, the only guiding principle being a desire to achieve representative recipes for both the O/W and W/O categories.

Microemulsions were prepared in hopes of using them as a medium for organic reactions. This is not a new idea; in the past decade several other groups have studied reactions in microemulsions [5]. Our own interest focused on exploiting microemulsions in a problem of considerable practical importance: the detoxification of mustard, a chemical warfare agent known since World War I and deployed even in modern times. Actually, mustard destruction constitutes a challenging problem in organic reactivity that goes far beyond mustard itself. But before elaborating on this point, it might be useful to state briefly why mustard presents such a threat to civilized society. Mustard is a vesicant that damages skin, eyes, and the respiratory tract. Blood cell forming tissues (marrow, lymph nodes, and spleen) are particularly sensitive to the cytotoxic alkylating properties of mustard. Small repeated doses are cumulative. Importantly, mustard can be synthesized by "garbage can chemistry" with commonly available reagents (1).



Purification of the final product is not necessary for those with evil intent. Owing to its ready availability, mustard has been called "the poor man's nuke". Although less toxic than nerve agents, mustard is much more "persistent" in the environment; compound lying on a water surface in the sunlight can remain unchanged for months.

We did not work directly with mustard but, instead, with the less dangerous half-mustard that manifests similar chemistry. Even half-mustard, however, should be handled with care in a hood.



Mustard detoxification exemplifies an extremely interesting and general problem in organic reactivity. Under laboratory conditions, where rates are usually measured at minute substrate concentrations, mustard is susceptible to hydrolytic deactivation. Thus, Swain in 1949 found a half-life of only 3 minutes at 25 °C in 5 % acetone-water [6]. How does this substantial reactivity coincide with the "persistent" nature of mustard that allows it to remain for months on a water surface? The answer lies in the low solubility of mustard in water (0.0043 M at 25 °C). Mustard dissolves so sparingly in water (and interfacial hydrolysis in a mustard-water slurry is so slow) that mustard resting upon a water surface persists for months, not minutes. Adding acid or base to the water further retards hydrolysis (perhaps because the elevated ionic strength further reduces the solubility). In the face of this problem, how can one achieve reasonable rates of mustard deactivation when environmentally realistic amounts of material are involved? I referred above to this being a general problem in organic reactivity because many inherently reactive and potentially dangerous compounds fail to react owing mainly to their insolubility.

The most obvious means for accelerating hydrolysis would be, seemingly, to solubilize the mustard in water with a surfactant. Surfactants in aqueous solutions form micellar aggregates that are capable of binding water-insoluble compounds such as mustards. Micellar catalysis subsequent to this binding is well documented [7]. Unfortunately, this tactic proved unsuccessful

with mustards ; micelle-solubilized mustard is virtually inert to hydrolysis. Apparently, the apolar substrate finds its way into the hydrocarbon core of micelles where formation of the ionic episulfonium ion (an intermediate in mustard solvolysis) is impeded. Although micelles solubilize mustard, they also kill the reaction.

The above considerations forced us to adopt another strategy, an oxidative one, for deactivating mustards. It was known that the sulfoxide corresponding to mustard is far less toxic than the parent sulfide. Thus, one could hope to oxidize mustard to its sulfoxide and hence remove the biological threat. Incidentally, since mustard sulfone is an irritant (although not as dangerous as mustard itself), further oxidation of the sulfoxide to the sulfone would be best avoided in any viable decontamination strategy.

Converting from a hydrolytic to an oxidative strategy avoids the need of solubilizing mustard in a water-rich medium. Thus, one could well imagine an oxidizing agent (e.g. *t*-butyl hydroperoxide) capable of reaching and destroying a sulfide even though the sulfide be buried in the hydrocarbon-like core of a micelle. But micelles have another serious difficulty that adversely affects their potential utility : they are able to solubilize only small amounts of substrate (1 mM or less under typical conditions). Macrocyclic hosts and cyclodextrins (currently popular for binding and solubilizing substances in water) are likewise deficient in solubilization capacity. We were, therefore, forced to adopt microemulsion systems which, as will now be demonstrated, allowed the dissolution and destruction of mustard at realistic and useful levels.

Microemulsions in *Table I* (15 mL samples) readily dissolve 1.45 mmol of both half-mustard and dibutyl sulfide. This corresponds to 0.18 mL and 0.25 mL of substrate, respectively. During the oxidations (described momentarily) a few of the microemulsions became cloudy, but this did not seem to impede the speed of the reaction. Up to a mL or more of mustard simulant is miscible in the microemulsions with > 10 % oil. As would be expected, the oil droplets in the O/W microemulsions, and the continuous phase in W/O microemulsions, are capable of dissolving large amounts of water-insoluble organic reactant.

Selection of a suitable oxidizing agent was the last major decision with regard to experimental conditions. Originally, the VO(acac)<sub>2</sub>-*t*-butyl hydroperoxide couple was called upon to affect oxidation. A typical system was composed of a microemulsion from *Table I* (15 mL), half-mustard (0.25 g, 2 mmol), *t*-butyl hydroperoxide (0.28 g, 2.2 mmol), VO(acac)<sub>2</sub> (0.038 g, 0.14 mmol), and acetic acid (0.2 mL). The homogeneous mixture was kept at room temperature and monitored by <sup>1</sup>H-NMR (as described below).

Reaction times (> 6 half-lives) for ME-1, ME-2 and ME-5 (to cite a few examples) were 36 min, 5 min and 60 min respectively. Ultimately, however, we abandoned this approach because :

- (a) We desired times faster than 5 min, our best value.
- (b) We found a simpler and cheaper oxidant, hypochlorite. Often, in modern synthetic methodology, expense is not mentioned, but in our case, as in real life, cost was an important consideration.

As already mentioned, oxidations were monitored by <sup>1</sup>H-NMR. Thus, the destruction of half-mustard could be observed from the decay of the reactant signals at 2.55 ppm (quartet) and 2.8 ppm (triplet) after diluting the sample in d<sub>6</sub>-acetone/CDCl<sub>3</sub>. Concomitant appearance of sulfoxide was evident from signals at 2.9 ppm (multiplet) and 3.1 ppm (triplet). If sulfone was also produced, then a signal centered at 3.38 ppm was observed. TLC on silica plates (hexane, ethyl acetate, ethanol, 4:2:1) confirmed the NMR analysis. Sulfoxide was isolated by column chromatography (46-88 % yield) with ME-2, ME-4, and ME-6. In our best reactions, the mustard simulant disappeared in the time required to quench the oxidation with NMR solvent (about 15 seconds). In such cases, we can only record an upper limit to the reaction time (< 15 s). This represents an extremely fast and generally useful protocol.

Upon discovering that hypochlorite oxidized our sulfides faster than did *t*-butyl hydroperoxide, even in the absence of a vanadium catalyst, we immediately switched over to the simpler and more efficient system. Oxidations were performed in the following manner. Aqueous hypochlorite (5 % as found in grocery store bleach) was added to half-mustard (0.18 mL) dissolved in 15 mL microemulsion. Oxidant was used in a 2-fold molar excess over sulfide. As seen in *Table II*, with many of the microemulsion systems the oxidation was complete in less than 15 seconds.

Several features of the mustard oxidation are worthy of mention :

1. The product is exclusively sulfoxide. Within the limits of NMR detection, no sulfone is formed. Selectivity of the microemulsion systems is beneficial from the point of view of converting mustard into the relatively non-toxic sulfoxide.
2. Reaction capacity is excellent, 15 mL of microemulsion being capable of oxidizing 0.18 mL of sulfide in a homogenous mixture. This represents a decided advantage over reactions promoted by micelles, cyclodextrin, and synthetic hosts that typically employ substrate levels of 1 mM or less [8]. An even larger scale oxidation was carried out by mixing the following components : dibutyl sulfide (1.5 mL, 8.7 mmol) ; 15 mL ME-2 or ME-6 ; and 24 mL 5.3 % aqueous hypochlorite. Although the composition of the original microemulsion was altered drastically by the large volume of water needed to provide sufficient oxidant, the mixtures remained homogenous, and the reactions occurred instantaneously. However, considerable amounts of sulfone (32-45 %) were formed. Conceivably, sulfone formation could be suppressed here by using a more concentrated hypochlorite solution (and hence less water), but the possibility has not yet been tested.
3. All components of the multi-component system are cheap and readily available. This is an important point, because the system is not catalytic (i.e. hypochlorite is consumed stoichiometrically) and because economics is a key consideration for use in the field if not in the laboratory.
4. The microemulsion systems circumvent laboratory conditions (heating, stirring, irradiation by light, etc.) that are debilitating for many practical applications. A scheme for decontaminating surfaces would, for example, fare badly if continuous stirring of an inhomogenous spray regimen were required.
5. Surface tensions of ME-2 and ME-8 are very low (24 and 22 dynes/cm) compared to that of water (72 dynes/cm) and mustard (42 dynes/cm). This means that the microemulsions will tend to

TABLE II. - Oxidation of half-mustard by sodium hypochlorite in microemulsion systems at 22 °C<sup>a</sup>.

Microemulsion <sup>b</sup>	Reaction Time <sup>c,d</sup>
1	< 15 s
2	5 min
3	< 15 s
4	< 15 s
5	< 15 s
6	< 15 s
7	> 6 h
8	< 15 s
9	> 6 h

<sup>a</sup> Half-mustard = 0.18 mL (1.45 mmol) ; NaOCl = 4.0 mL, 5.3 % bleach (2.9 mmol) ; 15.0 mL microemulsion.

<sup>b</sup> See *Table I*.

<sup>c</sup> Time for complete destruction of half-mustard (> 6 half-lives).

<sup>d</sup> Product is exclusively sulfoxide in all cases (no sulfone).

flow into cracks and crevices where toxic substances may be hiding. Water itself will not, of course, readily access such areas.

If the above list of attributes appears "applied" in nature and, perhaps, out of place here, then this is certainly not true for the most valuable aspect of our system: *speed*. Both basic and applied chemistry are intimately concerned with new methods for accelerating reactions. To judge the speed of our 15-second reaction time, consider the many months during which mustard can lie unchanged in direct contact with air, water, and sunlight. Although this may be an unfair comparison, it does show that mustard is not an inherently unstable molecule under environmental conditions. A better comparison would be between our microemulsion system and sulfide oxidation by hypochlorite *via* phase-transfer catalysis [9]. The best reported reaction time in this latter mode is 20 min. Not only is this much slower than the times in Table II, but phase-transfer catalysis requires stirring, a disadvantage in the real world as already mentioned.

Why is the microemulsion-based oxidation so fast? Examination of Table I and II shows that the nature of the surfactant is not critical. Anionic, non-ionic, and cationic surfactants (sodium dodecyl sulfate, Brij-96, and cetyltrimethylammonium bromide, respectively) are all effective. Reactions were "instantaneous" regardless of surfactant charge. Moreover, a < 15 second reaction time was observed with a "surfactantless" microemulsion. On the other hand, the cosurfactant appeared to play a necessary role apart from stabilizing the microemulsion. ME-7, an unusual microemulsion in that it lacks a cosurfactant, displayed only slow oxidation rates (> 6 h). ME-7 contained a unique surfactant, Aerosol-OT (AOT), but this cannot be the source of the slow rate because the oxidation was over in less than 15 seconds with a microemulsion consisting of: 56 % water, 24 % n-heptane, 8 % Aerosol-OT, and 12 % 1-butanol as the cosurfactant. We conclude that the cosurfactant actually participates in the chemistry of the oxidative process.

The most reasonable explanation for our results is that an alkyl hypochlorite [10] forms at the oil/water interface where the cosurfactant is known to reside (Figure 2). Subsequent oxidation

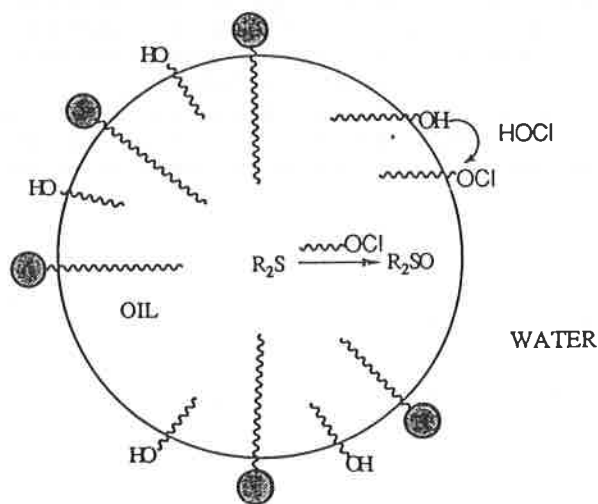


FIGURE 2. - Proposed mechanism for oxidation of an oil-soluble mustard by water-soluble hypochlorite mediated by a cosurfactant. The extremely fast rate is related in part to the large interfacial contact area between the oil droplet and the continuous aqueous phase.

of the half-mustard then proceeds either in or on the oil droplets. The speed of the sulfide oxidation can be attributed to a large hydrocarbon/water contact area that permits "communication" between the water-soluble HOCl and the oil-soluble sulfide with interfacial cosurfactant serving as an intermediary.

In summary, the microemulsion performs several functions:

- It solubilizes the water-insoluble substrate into a homogenous medium containing largely water.
- The oil microdroplets offer a huge surface area to the aqueous phase whereby guest substrates can come into contact with water-soluble reagents.
- The cosurfactant at the interface acts as a chemical messenger in the sense that it covalently accepts the oxidant ( $\text{Cl}^+$ ) and delivers it to the substrate in or on the microdroplet. The summation of the three effects leads to a remarkably fast and potentially useful reactivity. Other hydrophobic materials that contaminate the environment (DDT, PCB's, polycyclic aromatics, etc.) might also be amenable to destruction by microemulsion methods.

One last point should be made. The microemulsion represents a "community" of molecules that functions only by virtue of cooperative action. None of the five components (water, oil, surfactant, cosurfactant, and oxidant) can be omitted without loss of activity. Groups of molecules that operate collectively would seem to merit increased attention alongside the "single-molecule chemistry" that is already firmly established in halls of organic chemistry.

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